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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,981	05/07/2001	Charles D.Y. Sia	1038-1086 MIS:jb	6174

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,981	SIA ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Communication

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 26 March, 2004. Claims ~~1-11~~ 1-5 and 7-11 are pending in the instant application.

37 C.F.R. § 1.72

The abstract of the disclosure is objected to because it contains other material in addition to the abstract. It is noted that applicants provided a copy of the abstract published in PCT/CA99/00287. Applicants are reminded of the proper content of an Abstract of the Disclosure pursuant to § 608.01(b) of the M.P.E.P. The abstract must commence on a separate sheet and any sheet including an abstract or portion of an abstract may not contain any other parts of the application or **other material (37 C.F.R. § 1.72(b)).** Applicants are required to submit a new abstract on a separate sheet free of any other additional information.

37 C.F.R. § 1.98

The listing of references in the specification is not a proper information disclosure statement. 37 C.F.R. § 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and M.P.E.P. § 609 & A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited or considered by the examiner on a form PTO-892 or PTO-1449, they have not been considered.

35 U.S.C. § 112, Second Paragraph

Claims 1-11 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims have several deficiencies as follows: First, the reference to a "**T-helper molecule**" is vague and indefinite since the precise structural and functional characteristics of this "molecule" are not readily manifest. The disclosure fails to provide any further clarification concerning the intended claim language. Do the claims reference a polypeptide comprising a T-helper epitope (such as in a multideterminant polypeptide or vaccine) or are they directed toward an adjuvant (i.e., alum). These "molecules" all have different structures and functions. However, the specification fails to provide sufficient guidance pertaining to the metes and bounds of the patent protection desired. Second, the term "**T-cell inducing HIV-derived molecule**" is also vague and indefinite since it fails to set forth the precise structural and functional characteristics of the claimed "molecule" and how it is "derived" from HIV. Although the claims have been amended to specify that the "molecule" is a peptide comprising at least one T-cell epitope, nevertheless, it fails to provide any meaningful structural information. For instance, does the peptide comprise a T-helper or CTL epitope? Does the term "derived" allow for amino acid additions, deletions, or substitutions as compared to the parent HIV sequence? Third, the claims are directed toward the generation of an HIV-specific CTL response, yet the claims do not require the administration of a CTL epitope. Thus, the claimed methodology steps appear to be deficient since they fail to perform the stated objective. Perusal of the disclosure demonstrates that applicants generated HIV-1 Rev-specific CTL responses by administering a polypeptide consisting of

a T-helper epitope (e.g., CLP-243:HBV NC) and another polypeptide consisting of an HIV-1 Rev CTL epitope, or lipopolypeptides comprising the same. The inclusion of various adjuvants was also discussed. Different immunization regimens were employed (i.e., prime-boost with peptide, lipopeptide, etc.). Appropriate revision of the claim language is required. Applicants' arguments have been carefully considered but are not deemed to be persuasive for the reasons set forth *supra*.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *University of Rochester* v. *G. D. Searle & Co., Inc.*, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C. 2004). To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935

F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of "**T-helper molecules**" and "**T-cell inducing HIV-derived molecule**". An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). **The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.**

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently

detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., **complete or partial structure**, other physical and/or chemical properties, **functional characteristics when coupled with a known or disclosed correlation between function and structure**, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or **amino acid sequence**, chemical structure, **binding affinity**, **binding specificity**, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

The claims of the instant application are broadly directed toward a large genus of molecules comprising "T-helper molecules" and "T-cell inducing HIV-derived molecules". Concerning the first

group, the disclosure describes a single polypeptide T-helper cell epitope obtained from the HBV NC. This epitope consists of the following amino acid sequence: NH_2-TPPAYRPPNAPIL-COOH. This is the only T-helper epitope disclosed in the specification. The disclosure does not provide any structural or functional guidance pertaining to other suitable T-helper molecules, irrespective of their chemical structure. Furthermore, while the disclosure provides a limited number of specific **HIV-1_{LAI} Rev CTL-epitopes** (e.g., SEQ ID NOS.: 3, 5, and 8, which correspond to amino acids 65-75, 78-87, and 102-110), it fails to provide any other HIV-1 or -2 "T-cell epitopes" or molecules derived from said epitopes. The disclosure fails to provide any meaningful structural of functional information concerning these epitopes and molecules. Accordingly, the skilled artisan would reasonably conclude that applicants were clearly not in possession of the full genus of compounds.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of

the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-5, 7, and 11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over van Baalen *et al.* (2000) in view of Thornton *et al.* (1989). van Baalen and colleagues provide HIV-1 Rev CTL epitopes, or T-cell inducing HIV derived molecules, that correspond to SEQ ID NOS.: 3 and 8 (see Table II) set forth in the instant application. This teaching provides immunogenic compositions comprising the polypeptides of interest, various immunizing formulations, and suitable adjuvants (see cols. 7 and 8). This teaching does not disclose the administration of another polypeptide comprising a T-helper epitope along with the CTL epitopes described.

However, Thornton and associates provide a T-helper epitope, or T-helper molecule, obtained from the HBV NC and methods of using the same to induce strong immune responses against the immunogen of interest. Moreover, the T-helper epitope identified corresponds to CLP-243 (see Table I, col. 14; col. 32; col. 33; col. 36). The authors state unambiguously (see col. 17) that "The HBcAg T cell epitope containing polypeptides can be used to enhance the immunogenicity of a polypeptide immunogen, preferably a pathogen related immunogen."

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare an immunogenic composition comprising both a "T-helper molecule", such as the T-helper epitope provided by Thornton *et al.* (1989), and a "T-cell inducing HIV-derived molecule" such as the HIV-1 Rev CTL epitopes provided by van Baalen *et al.* (2000), and to

use said composition to induce strong immune responses against the CTL epitopes of interest. The skilled artisan would have both a reasonable expectation of success and the motivation to do so, because Thornton and colleagues clearly demonstrate that T-helper molecules are useful accoutrements for the development of a strong immune response. One of ordinary skill in the art would have been further motivated to utilize other art-recognized adjuvants (e.g., ALUM) and immunization regimens (i.e., prime-boost) to obtain the optimal immune response.

Claims 8-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over van Baalen *et al.* (2000), in view of Thornton *et al.* (1989), as applied *supra* to claims 1-5, 7, and 11, and further in view of Chisari *et al.* (1998). Neither van Baalen *et al.* (2000) or Thornton *et al.* (1989) disclose the preparation of lipopeptides comprising the "T-cell inducing HIV-derived molecule" of interest. However, Chisari and colleagues identify various HBV CTL epitopes and report that these peptides can be conjugated to various lipid moieties that enhance the immune response to the CTL of interest (see cols. 15-16). Specifically, it was reported that "Lipids have been identified which are capable of priming CTL *in vivo* against viral antigens,..., which can effectively prime virus specific cytotoxic T lymphocytes when covalently attached to an appropriate peptide...Peptides of the invention can be coupled to P_3CSS", for example, and the lipopeptide administered to an individual to specifically prime a cytotoxic T lymphocyte response" (col. 15, lines 57-66).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to conjugate a "T-cell inducing HIV-derived molecule" such as one of the HIV-1 Rev CTL epitopes provided by van Baalen *et al.* (2000), to a lipid moiety (e.g., palmitoyl), as provided Chisari and

coworkers, since this would reasonably be expected to increase the immunogenicity of the CTL epitope of interest.

Non-statutory Double Patenting

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 U.S.P.Q. 644 (C.C.P.A. 1969); *In re Vogel*, 422 F.2d 438, 164 U.S.P.Q. 619 (C.C.P.A. 1970); *In re Van Ornum*, 686 F.2d 937, 214 U.S.P.Q. 761 (C.C.P.A. 1982); *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985); and *In re Goodman*, 29 U.S.P.Q.2d 2010 (Fed. Cir. 1993). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. § 3.73(b).

Claims 1-5 and 7-11 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4-15 of copending Application No. **09/055,744** in view of van Baalen *et al.* (2000). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). *In re Berg*,

140 F.3d 1428, 46 U.S.P.Q.2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 U.S.P.Q.2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '744 application are similar to those of the instant application except for the MHC class I restriction requirement. However, van Baalen and associates clearly provide HLA-A2 HIV-1 Rev CTL epitopes (see Table II). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use these CTL epitopes to induce a CTL response in the appropriate MHC-restricted (e.g., HLA-A2) population.

This is a **provisional** obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized

Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

06 September, 2005